Novel Rearrangements of Enynes Catalyzed by $PtCl_2$

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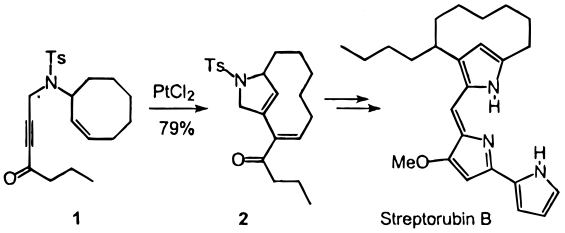
Pioneering studies of Murai et al. have shown that $PtCl_2$ is a versatile catalyst for intramolecular skeletal rearrangements of enynes.[1] These substrates convert (i) into 1,3-dienes via a formal enyne metathesis,[1,2] (ii) into 1,4-dienes if the alkene group is part of an allylsilane (stannane) entity,[3] or (iii) into polycyclic arrays if dienynes are used as starting materials.[4]



These operationally simple reactions result in a significant increase in molecular complexity which enabled, e.g., an efficient total synthesis of the immunosuppressive pyrrole alkaloid streptorubin B via a $PtCl_2$ catalyzed conversion of the electron deficient enyne **1** into *meta*-pyrrolophane derivative **2**.[5] Strong evidence has accumulated that this key step proceeds through a *cationic* mechanism triggered by the coordination of Pt(II) onto the alkyne group of the substrate.[5,6]

In pursuit of this result, however, we noticed that seemingly closely related 1,6-enynes can also feed an entirely different pathway. While the terminal monocyclic enyne **3** provides the *meta*-bridged bicyclic compound **4** via the expected formal enyne metathesis,[7,8] truncated substrate **5** delivers only 2% of 1,3-diene **7** but yields the previously unknown cyclopropane derivative **6** as the major product.[9] If enyne **8** is exposed to $PtCl_2$ in toluene at 80 °C, both reaction channels are operative to a similar extent, which may indicate a common reactive intermediate. The unusual structure of the tricyclic compound **9** was confirmed by high-resolution NMR and X-ray crystallography (see the Supporting Information).

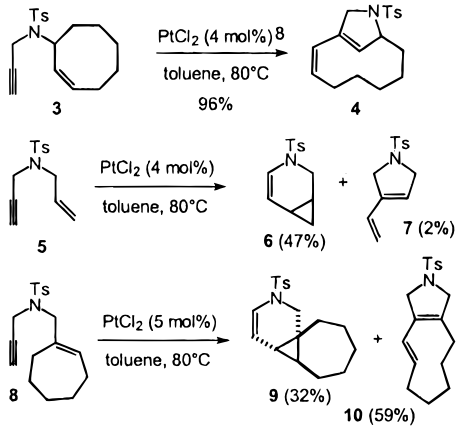


Table 1 compiles additional substrates undergoing formal enyne metathesis. As can be seen, substantial structural variations are possible and the reaction is by no means limited to compounds in which the alkene group is part of a (strained) preexisting ring (entry 1). Electron withdrawing groups at the alkyne facilitate the transformation (entries 3 and 4),[5] and remote alkenes are tolerated (entry 6). In contrast, however, all cases recorded so far delivering bicyclo[4.1.0] heptene derivatives (Table 2) use enynes containing a heteroatom in the tether. Even allylsilanes follow this path, although substrates of this type lacking the heteroatom were recently described to undergo $PtCl_2$-catalyzed transformations into 1,4-dienes.[3] One may speculate that the stability of the resulting enamides or enolethers contributes to the formation of these products.

Although an unambiguous mechanistic interpretation of these complex reorganizations of C−C bonds must await further studies,[10] it is possible to explain the formation of both types of products via a cationic manifold similar to the one operative in the conversion **1** → **2**.[5] Complexation of Pt(II) renders the alkyne susceptible to nucleophilic attack by the tethered alkene.[6] The resulting delocalized cation represented by forms **A**−**D** stabilizes along two different pathways as formally depicted in Scheme 1. While the evolution of its cyclobutyl cation form **B** leads to 1,3-dienes as the products of a formal enyne metathesis,[11] the cyclopropyl-methyl structure **C** is "carbenoid" in nature and suffers a hydrogen shift to give the enamide (X = NR) or enol ether (X = O) products.

Next, we attempted to intercept the assumed electrophilic Pt(II)−alkyne complex by nucleophiles other than alkenes. For this purpose we designed ether derivatives of the general structure shown in Scheme 2 in which coordination of the metal may trigger a cascade comprising a 1,4-addition of the ether oxygen onto the complexed alkyne and simultaneous release of a (metal complexed) allyl cation. Recapturing this fragment by the emerging organoplatinum intermediate then leads to a subsequent C−C bond formation.

In fact, substrates of this type smoothly undergo this previously unknown O → C allyl shift on exposure to catalytic amounts of $PtCl_2$ in toluene as the preferred solvent (Scheme 3). Good yields and high degrees of stereoselectivity in favor of the (*E*)-isomer were observed.[12] Moreover, the formation of products **14** and **15**

(1) (a) Chatani, N.; Furukawa, N.; Sakurai, H.; Murai, S. *Organometallics* **1996**, *15*, 901. (b) For similar reactions catalyzed by Ru catalysts see: Chatani, N.; Morimoto, T.; Muto, T.; Murai, S. *J. Am. Chem. Soc*. **1994**, *116*, 6049. (c) See also: Trost, B. M.; Chang, V. K. *Synthesis* **1993**, 824.

(2) Similar enyne metatheses catalyzed by palladol complexes have also been described. They are believed to proceed via a Pd(II)/Pd(IV) manifold involving palladacyclopentene and cyclobutene intermediates, cf.: (a) Trost, B. M.; Trost, M. K. *J. Am. Chem. Soc*. **1991**, *113*, 1850. (b) Trost, B. M.; Yanai, M.; Hoogsteen, K. *J. Am. Chem. Soc*. **1993**, *115*, 5294.

(3) Fernandez-Rivas, C.; Méndez, M.; Echavarren, A. M. *J. Am. Chem. Soc*. **2000**, *122*, 1221.

(4) Chatani, N.; Kataoka, K.; Murai, S.; Furukawa, N.; Seki, Y. *J. Am. Chem. Soc*. **1998**, *120*, 9104.

(5) Fürstner, A.; Szillat, H.; Gabor, B.; Mynott, R. *J. Am. Chem. Soc*. **1998**, *120*, 8305.

(6) For the carbocation-like behavior of Pt(II)−alkyne complexes see: Chisholm, M. H.; Clark, H. C. *Acc. Chem. Res*. **1973**, *6*, 202.

(7) Review: Mori, M. *Top. Organomet. Chem*. **1998**, *1*, 133.

(8) Commercial $PtCl_2$ was used as received. Only in the case of substrate **3** reaction with commercial $PtCl_2$ gives a complex mixture as described in ref 5. In this case, $PtCl_2$ prepared by heating of $PtCl_4$ at 300 °C in vacuo was found to effect a very clean conversion into the desired product **4**.

(9) A similar transformation catalyzed by $PtCl_4$ was described for allyl propargyl ethers; in most cases, however, the yields obtained were rather low. Conversion of the alkyne into an allene followed by formation of a metallacycle was proposed as the reaction mechanism, cf.: Blum, J.; Beer-Kraft, H.; Badrieh, Y. *J. Org. Chem*. **1995**, *60*, 5567.

(10) All attempts to detect intermediates by means of NMR have failed so far even if stoichiometric amounts of $PtCl_2$ were used.

(11) One can envisage that intermediate **B** either evolves as indicated in Scheme 1 or converts into a cyclobutene derivative, which then undergoes an electrocyclic ring opening; note that both pathways deliver the same 1,3-diene product. If a cyclobutene is assumed as a discrete intermediate, the mechanism resembles the late steps of the mechanism proposed by Trost (ref 2), which differs conceptually from ours, however, in the assumed formation of a palladacycle as the triggering event.

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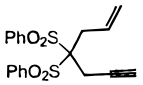
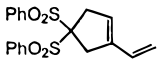
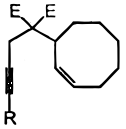
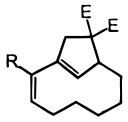
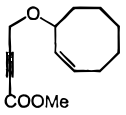
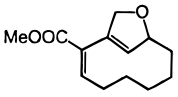
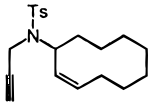
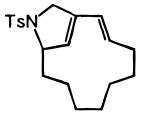
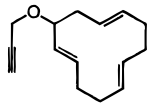
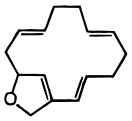
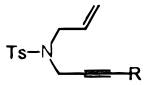
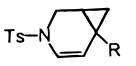
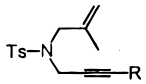
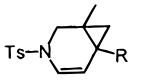
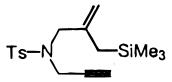
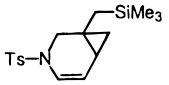
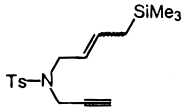
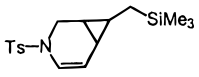
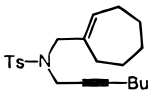
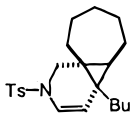
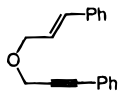
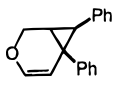
Table 1. Enyne Metathesis Reactions Catalyzed by $PtCl_2$[a]

Nr	Substrate	Product	Yield
1			96%
2			83% (R = H)[b]
3			63% (R=C(O)Me)[b]
4			70%
5			80%
6			54%

[a] In toluene at 80 °C using 4−10 mol % of $PtCl_2$. [b] E = COOEt.

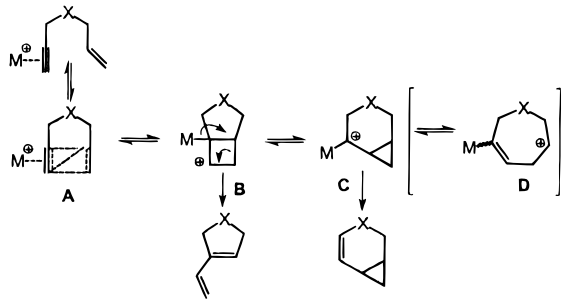
Table 2. Formation of Cyclopropane Derivatives Catalyzed by $PtCl_2$[a]

Nr	Substrate	Product	Yield[b]
1			59% (R = Me)
2			78% (R = Ph)
3			68% (R = H)
4			69% (R = Me)
5			73%
6			76%
7			87%
8			83%[9]

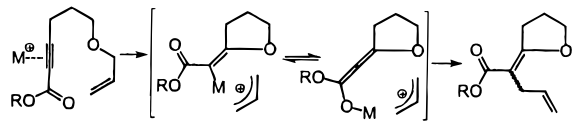
[a] In toluene at 60−80 °C using 4 mol % of $PtCl_2$. [b] Small amounts (1−15%) of the corresponding 1,3-dienes resulting from formal enyne metathesis of the substrates were obtained as byproducts in all cases.

from substrate **13** as well as of the rearranged compound **17** from enyne **16** indicates that an allyl cation equivalent intervenes at some stage of the reaction and thereby supports the mechanistic rationale outlined above.

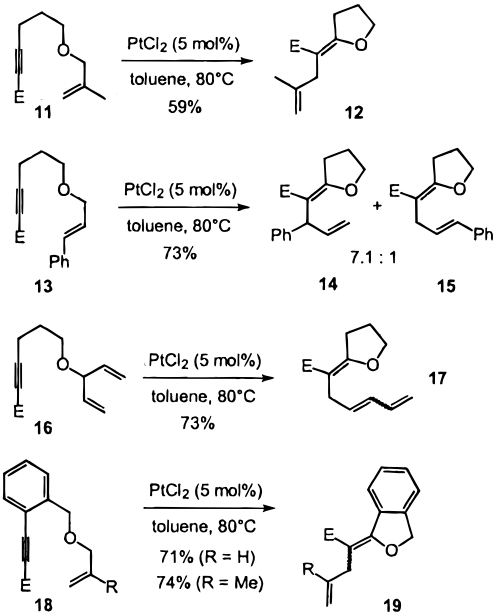
Scheme 1



Scheme 2



Scheme 3



Further studies on the scope and mechanism of these and related reactions are underway and will be reported in due course.[13]

Acknowledgment. Generous financial support by the DFG (Leibniz Program) is acknowledged with gratitude. F.S. thanks the Fonds der Chemischen Industrie for a Kekulé stipend. We thank the Degussa-Hüls AG for a generous loan of $PtCl_2$.

Supporting Information Available: Representative procedures, spectroscopic and analytical data of all new products, and X-ray structure of product **9** (PDF). This material is available free of charge via the Internet at http://pubs.acs.org.

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(12) Compounds **12**, **14**, **15**, and **17** were obtained as pure (*E*)-isomers with respect to the configuration of the exocyclic double bond; in the case of product **19**, however, the (*Z*)-isomer is formed as a byproduct (R = Me, *E*:*Z* = 10.3:1; R = H, *E*:*Z* = 2.4:1). The fact that (*E*,*Z*)-mixtures are obtained in these cases seems to rule out a concerted mechanism.

(13) See also: Fürstner, A.; Voigtländer, D. *Synthesis* **2000**, 959.